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ARMY MEDICAL RESEARCH LABORATORY

FORT KNOX, KENTUCKY

REPORT NO. 139

12 February 1954

EFFECT OF PARTIAL SHIELDING BY GRIDS ON SURVIVAL OF X-IRRADIATED RATS

*Subtask under Biological and Medical Aspects of Ionizing Radiation,
AMRL Project No. 6-59-08-014, Subtask, Effects of Ionizing Ra-
diation.

RESEARCH AND DEVELOPMENT DIVISION
OFFICE OF THE SURGEON GENERAL
DEPARTMENT OF THE ARMY



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**EFFECT OF PARTIAL SHIELDING BY
GRIDS ON SURVIVAL OF X-IRRADIATED RATS**

by

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from

**ARMY MEDICAL RESEARCH LABORATORY
FORT KNOX, KENTUCKY
12 February 1954**

***Subtask under Biological and Medical aspects of ionizing radiation,
AMRL Project No. 6-59-08-014, Subtask, Effects of Ionizing Ra-
diation.**

Report No. 139
Project No. 6-59-08-014
Subtask AMRL S-1
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ABSTRACT

EFFECT OF PARTIAL SHIELDING BY GRIDS ON SURVIVAL OF X-IRRADIATED RATS

OBJECT

To determine whether or not irradiation of entire animals through grids is less effective in producing lethality than direct total body irradiation and whether there is a relation between effectiveness and grid hole size.

RESULTS

Exposure of rats to equal volume doses of x-radiation (200 kg roentgens) through grids having various diameter hole size but a constant open area to closed area ratio resulted in increasingly greater survival as the hole size was decreased. Significantly greater survival was obtained in animals exposed through grids than in animals directly exposed to total body irradiation of equal volume dosage.

CONCLUSION

The increased survival found in rats exposed through grids probably results from repair initiated in the irradiated areas by adjacent normal tissue. The observation that survival was directly related to the area of the interface between normal and irradiated tissue supports the concept of a local effect of shielding. It appears that under the proper conditions the local effects may be more beneficial than the remote effects in protecting animals from radiation.

RECOMMENDATIONS

Because of the possible fundamental value of the concept of the local effects of partial shielding these studies should be extended to include a greater range of grid hole size, various geometrical shapes of grid holes, various ratios of open to closed areas, various sized experimental animals, and histological studies on mechanisms by which the local effect is produced.

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EFFECT OF PARTIAL SHIELDING BY GRIDS ON SURVIVAL OF X-IRRADIATED RATS

I. INTRODUCTION

There appear to be at least two general mechanisms by which partial body shielding protects animals from x-radiation. The first of these, which may be termed "remote" effect, has been thoroughly investigated by a number of workers (1-7). In studies on this mechanism of protection a single organ or portion of the body is shielded with lead and the "remote" effects such as effect on survival, white cell count, rate of regeneration of the marrow, etc., are studied. Whether or not the results can be explained by a humoral substance (1), cell seeding (1, 6, 7), or a tiding over of the animal's defense mechanisms (6) is not yet established. In any event it is clear that repairative processes are stimulated at a distance from, but under the influence of, the shielded normal tissue.

The second general mechanism may be called the "local" effect of shielding. Here the area of interest is located at the interface between shielded and irradiated tissues. Kohler (8) Liberson (9), Goldfeder (10), Grynkrant (11), Jolles (12), Marks (13), and others have shown that when radiation is delivered through multiple holes in a shielding material, i. e. through a grid, doses which would not ordinarily be tolerated by the skin if given over the entire area can be delivered with relative safety. It is generally believed that this phenomenon can be best explained on the basis of the normal shielded skin (9, 14) and/or connective tissue (11) adjacent to the irradiated tissue initiating repair of the damaged area. No information is available as to whether this protective effect is limited to the skin and underlying connective tissue or is a property of tissues in general which might be utilized to protect animals against total body irradiation.

The present study was undertaken to determine whether or not irradiation of entire animals through a grid is less effective in producing lethality than direct total body irradiation and if so, to determine the relation of effectiveness to grid hole size.

II. EXPERIMENTAL

A. Methods

A total of 104 adult male Sprague-Dawley rats weighing 250 ± 25 gms each were used in the present study. Prior to and following irradiation the rats were housed 2 or 3 to a cage and given water

and Purina Laboratory Chow ad libitum. The rats were anesthetized with pentobarbital prior to radiation exposure. They were then placed, 2 at a time, on their left sides in a shallow lucite cage. A lucite lid, with or without a lead grid attached, was placed on top of the cage in close proximity to the surface of the rats. Following radiation exposure the animals were observed daily for 30 days and the survival noted.

The grids used in the present study were constructed from lead sheets 1.6 mm thick. Previous measurements showed that lead of this thickness transmitted only 1 per cent of the incident radiation dose. The closed to open areas were kept constant at 60 to 40 per cent, respectively, and only the hole size was varied. The holes were distributed as uniformly as possible over a circular area of 189 cm².

X-rays were delivered from a Keleket Deep Therapy Model machine operated at 200 KVP and 9 ma with added filters of 1.0 mm Al and 0.5 mm Cu. The target-specimen distance was 29.5 cm and the dose rate 62.0 r/min measured in air. The grid transmission dose rates were measured by rotating a Victoreen ionization chamber under the grids on an eccentric axis. Data on hole sizes, transmission rates, etc. for the various grids are given in table 1. To determine the approximate extent of scatter of the radiation in passing through a rat, films were placed immediately beneath the grid and immediately beneath the rats. The assembly was then exposed to radiation. The results of this study indicated that scattering was minimal and that when a grid was used the radiation was delivered essentially as sharply defined cylinders (Fig. 1).

TABLE 1
PHYSICAL DATA ON GRID HOLE SIZES, PERCENT OPEN AREA,
AND DOSE RATES TRANSMITTED

Shielding	Hole Size (diam. cm)	Hole Area (cm ²)	Distance Between Centers (Cm)	Calculated % Open Area	Measured % Open Area	Dose Rate Through Grid (r/min)
None (open portal)	---	---	---	100%	100%	62.0
Grid 1	1.0	0.79	1.40	40%	48%	28.9
Grid 2	0.66	0.34	0.93	40%	46%	27.5
Grid 3	0.44	0.15	0.61	40%	42%	26.2
Grid 4	0.32	0.08	0.44	40%	46%	26.6



A



B

FIG. 1 X-RAY OF GRID, WITH (A) FILM BELOW RAT
(B) FILM ABOVE RAT.

Since rats exposed through the grid received only about 40% of the dose incident to the grid it was necessary to compensate for this lower dose rate to the shielded animals by increasing the exposure times. For this purpose the concept of volume dose as discussed by Hempelmann *et al* (15) was used. According to these authors the integral or volume dose "is the product of the radiation dose in energy units multiplied by the mass of irradiated tissue in grams". The unshielded control rats (av. wt. 250 gms) were given a total body exposure of 800 r or an average volume dose of 200 kilogram roentgens per rat. Only 40% or about 100 gms of the rats irradiated through the various grids were exposed to radiation. To make the total energy absorption or average volume dose per rat equal to the dose received by the controls it was necessary to increase the dose incident through the holes in the grids to 1750 r. Since this dose was based on the actual measured transmissions for the various grids it is apparent that the average volume dose was identical for all groups and was independent of the minor variations actually encountered from the calculated value of 40% open area (Table 1).

B. Results

Exposure of rats to equal volume doses of x-radiation through grids having various diameter hole sizes but a constant open area to closed area ratio resulted in increasingly greater survival as the hole size was decreased. These data are shown in Table 2 and Figures 2 and 3. Of the 24 control rats exposed to a total body radiation dose of 800 r (or 200 kilogram roentgens volume dose) only 5 or 21% survived for 30 days. Rats irradiated with the same volume dose (2000 r to 40% of the body or 200 kg roentgens) showed no increase in survival when the radiation was delivered through a grid having holes 1 cm in diameter. When the hole sizes were reduced to 0.66, 0.44, and 0.32 cm in diameter, however, 30 day survivals of 37, 68, and 84 per cent, respectively, were found. In Figure 3, per cent survival is plotted against log of hole areas. The resulting straight line indicates a simple exponential relationship over the range of hole sizes studied.

TABLE 2
EFFECT OF X-IRRADIATION THROUGH VARIOUS GRIDS ON SURVIVAL OF RATS

Shielding	Hole Size (Diam. cm.)	No. Rats	Volume Dose (kilogram roentgens/ 250 gm rat)	30 Day Survival	% Survival
None	---	24	200	5	21
Open portal					
Grid 1	1.0	19	200	3	16
Grid 2	0.66	19	200	7	37
Grid 3	0.44	19	200	13	68
Grid 4	0.32	19	200	16	84

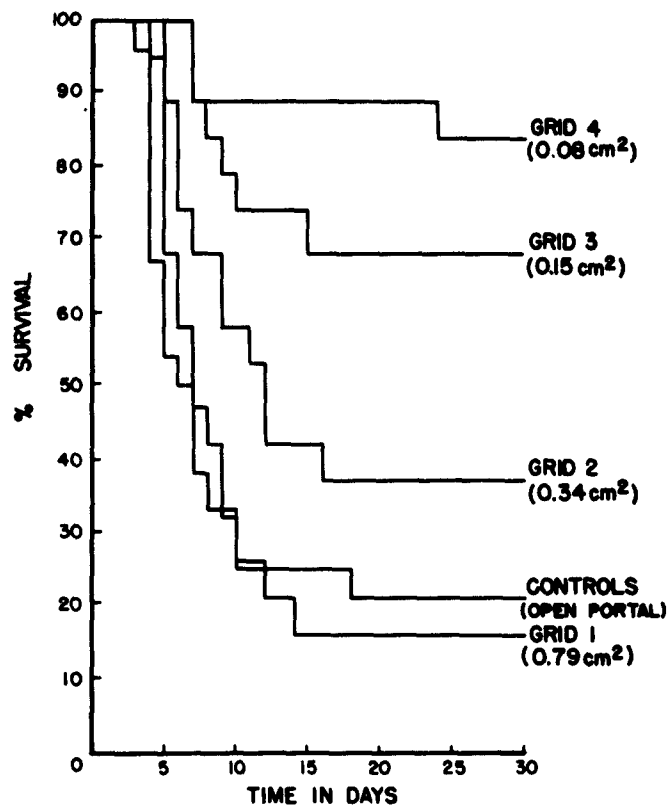


FIG. 2 SURVIVAL OF RATS EXPOSED TO EQUAL VOLUME DOSES OF X-RAYS THROUGH GRIDS WITH VARIOUS HOLE SIZES.

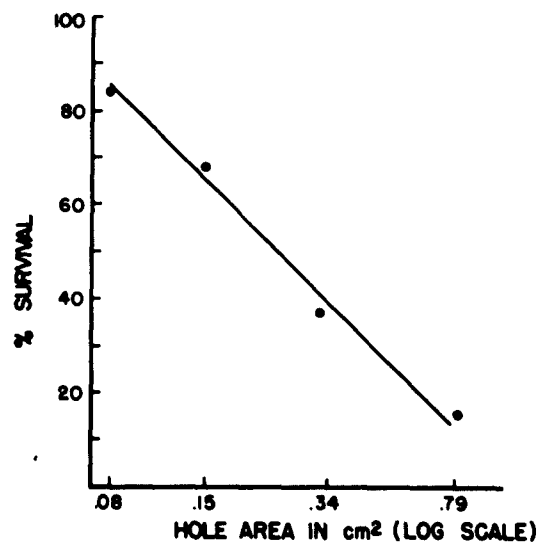


FIG. 3 RELATION OF GRID HOLE AREAS TO SURVIVAL OF RATS GIVEN EQUAL VOLUME DOSES OF X-RAYS.

III. DISCUSSION

Exposure of rats to x-radiation delivered through grids has been shown, in the present study, to increase survival significantly over that found in control rats exposed to equal volume doses to total body x-irradiation. Grid hole size was found to be of critical importance in altering survival. Rats exposed through grids having openings of 0.66 cm or less in diameter showed increasing survival with decreasing hole sizes even though the ratio of total open area to closed area was kept constant at a 40 to 60 per cent ratio.

Other investigators have found similar protection of skin and underlying connective tissue of men and experimental animals when radiation was delivered through a grid (8-14). Presumably this protective effect, which may be called the local effect of partial shielding as opposed to the remote effects obtained by spleen or marrow shielding, may be explained as being due to the initiation of repair in the irradiated area by the surrounding unirradiated tissues. This conclusion is supported by the fact that greater protection was obtained as hole sizes in the grids were decreased. Such decrease in size had the effect of increasing the total area of the interface between irradiation and normal tissues. If protection is due to reparative changes induced at these interfaces then it would be expected that degree of protection would be related to interface area. The data obtained in the present study showed such a relationship (Table 2 and Figures 2 and 3).

It should be pointed out that this theory may be further tested by changing the shape of the openings in the grids while maintaining the area of the openings constant. Circular holes should give minimum protection since the perimeter to area ratio is much smaller than the perimeter to area ratio of other geometrical shapes such as the squares and rectangles that are used by clinical radiotherapists. Further study on this point is indicated.

The possibility that the protective effect obtained in the present study was exerted remotely by protection of hematopoietic and/or lymphatic tissue must be considered. Since the areas of the rat that were shielded were randomly distributed and in each case amounted to 60% of the animal it is apparent from the laws of probability that approximately 60% of the bone marrow, spleen, lymphatic tissue, etc. were protected. If protection had been obtained by the remote effects of shielding these tissues then no difference in survival with grid openings of various sizes would be expected. Since differences were found it must be concluded that the protective effect could not be explained on this basis.

Studies in which large single areas of animals have been shielded and the remainder exposed to radiation have shown that in general there is a fairly specific threshold of dosage which cannot be exceeded if the animal is to survive (3). This threshold presumably represents the level at which remote effects of shielding are no longer effective and direct irreversible damage to vital tissues leads to death. The present study suggests that the local effect of shielding may be effective in protecting animals at doses in excess of those at which the remote effects are operative. It seems likely, on the basis of these considerations, that shielding of a given percentage of an animal by a grid may be preferable to shielding a similar percentage of an animal by a single solid sheet of protective material.

IV. SUMMARY AND CONCLUSIONS

Exposure of rats to equal volume doses of x-radiation (200 kg roentgens) through grids having various diameter hole sizes but a constant open area to closed area ratio resulted in increasingly greater survival as the grid hole sizes were decreased. Significantly greater survival was obtained in rats exposed through grids than in rats exposed to total body x-irradiation. It is suggested that these results may be explained as being due to a beneficial local effect of partial shielding whereby normal tissue adjacent to irradiated tissue initiates repair in the irradiated areas. Degree of survival appeared to be directly related to the area of interface between normal and irradiated tissue.

V. RECOMMENDATIONS

Because of the possible fundamental value of the concept of the local effects of partial shielding these studies should be extended to include:

1. Studies with grids with even smaller hole sizes to determine the maximum degree of protection obtainable.
2. Studies with grids having holes of various shapes to determine the optimum area-perimeter ratio.
3. Studies with various sized animals to determine whether there is a relation between body size and optimum hole size.
4. Studies with various ratios of open to closed areas to determine the optimum ratio.

5. Studies with various total x-ray dosages to determine absolute changes in the LD₅₀.

6. Histopathological studies to study the mechanisms by which the local effect is produced.

VI. BIBLIOGRAPHY

1. Jacobson, L. O. , E. L. Simmons, E.K. Marks, M. J. Robson, W.F. Bethard, and E.O. Gaston. The role of the spleen in radiation injury and recovery. J. Lab & Clin. Med 35: 746, 1950.
2. Edelman, A. Adrenal cortex and survival of rats after x-irradiation. Fed. Proc. 9: 36, 1950.
3. Bond, V.P. , M.N. Swift, A.C. Allan, and M.C. Fishler. Sensitivity of abdomen of rat to x-irradiation. Am. J. Phys. 161: 323, 1950.
4. Gershon - Cohen, J. , H. B. Hermel, and J. Q. Griffith. Protective effect of small lead shields during repeated whole-body x-ray irradiation of rats. Radiol. 58: 383, 1952.
5. Lamerton, L.F. , L.A. Elson, and E.B. Hariss. A study of the phases of radiation response in the rat. II. The effects of non-uniform irradiation. Brit. J. Radiol. 26: 560, 1953.
6. Storer, J.B. , C.C. Lushbough, and J.E. Furchner. The protective effect of shielded ectopic bone marrow against total body x-radiation. J. Lab & Clin. Med. 40: 355, 1952.
7. Czerwonka, O. , J. Gregg, W. Parr, W. Luther and A. Krebs. A study of mitotic activity in the intestinal epithelium of the albino rat and it's role in the recovery process after x-radiation. M.S.F.R.L. Project No. 6-64-12-06-(40), 25 November 1950.
8. Kohler, A. Zur Roentgentherapie Mit Massendosen. Muchen Med. Wchnschr. 56: 2314, 1909.
9. Liberson, F. Value of multi -perforated screen in deep x-ray therapy. Radiol. 20: 186, 1933. Critical study of use of lead perforator and reciprocal in radiation therapy. Am. J. Roent. 36: 245, 1936.

10. Goldfeder, A. Physical and biological aspects of radiation therapy. J. Am. M. Women's A. 5: 129, 1950.
11. Grynkrut, B. Direct and indirect radiotherapy. Am. J. Roent. 53: 491, 1945.
12. Jolles, B. Study of connective tissue reaction to radiation: The sieve or chess method. Brit. J. Cancer 3: 27, 1949. The sieve in radiotherapy. Brit. J. Radiol. 25: 395, 1952. Reciprocal vicinity effect of irradiated tissues on "diffusible substance" in irradiated tissues. Brit. J. Radiol. 23: 18, 1950.
13. Marks, H. New approach to roentgen therapy of cancer with use of grid (preliminary report). J. Mt. Sinai Hosp. 17: 46, 1950.
14. Jacobson, L. E. Grid depth dose investigation for 200 and 400 kilovolts at the center and edge of the field. Am. J. Roent. 69: 991, 1953.
15. Hempelmann, L. H., H. Lisco, and J. G. Hoffman. The acute radiation syndrome: A study of nine cases and a review of the problem. Ann. Int. Med. 36: 279, 1952.